

CLAIMS

We claim:

1. A composition which comprises delivery vehicles; said delivery vehicles having a mean diameter in the range of 50-300 nm and having stably associated therewith at least one therapeutic agent and at least one drug resistance modulator, or at least two drug resistance modulators, wherein the therapeutic agent and the drug resistance modulator or the two drug resistance modulators in combination exhibit a biologic effect to a drug resistant target.
2. The composition of claim 1 wherein the biologic effect is non-antagonistic.
3. The composition of claim 1 wherein the therapeutic agent and the drug resistance modulator or the two drug resistance modulators are at a ratio that exhibits a non-antagonistic biologic effect to a drug resistant target.
4. The composition of claim 3 wherein the non-antagonistic biologic effect is a potentiating biologic effect.
5. The composition of claim 3 wherein the non-antagonistic biologic effect is a synergistic biologic effect.
6. The composition of claim 1 wherein the therapeutic agent is an antineoplastic agent.
7. The composition of claim 1 wherein the drug resistance modulator is a drug efflux pump inhibitor.
8. The composition of claim 7 wherein the drug efflux pump inhibitor is an inhibitor of p-glycoprotein.
9. The composition of claim 1 wherein the therapeutic agent and the drug resistance modulator in combination provide a therapeutic effect greater than either agent alone.

10. The composition of claim 1 wherein the therapeutic agent and the drug resistance modulator in combination provide a therapeutic effect to a tumor that is resistant to a first-line drug treatment.

11. The composition of claim 1 wherein said therapeutic agent is an anti-microbial agent.

12. The composition of claim 1 wherein therapeutic agent is an anti-viral agent.

13. The composition of claim 1 wherein the delivery vehicles have a circulation half-life of at least 2 hours.

14. The composition of claim 1 wherein the delivery vehicles are liposomes.

15. The composition of claim 14 wherein the liposomes are selected from the groups consisting of multilamellar vesicles (MLVs), large unilamellar vesicles (LUVs) and interdigitating fusion liposomes.

16. The composition of claim 14 wherein the liposomes comprise a stabilizing lipid.

17. The composition of claim 14 wherein the liposomes are not prepared by sonication.

18. The composition of claim 14 wherein the liposomes do not contain cardiolipin.

19. The composition of claim 1 wherein the therapeutic agent is not doxorubicin.

20. The composition of claim 1 wherein the delivery vehicles are nanoparticles.

21. A composition which comprises delivery vehicles, said delivery vehicles having stably associated therewith two or more drug resistance modulators.

22. The composition of claim 21 further comprising a therapeutic agent.
23. The composition of claim 22 wherein the therapeutic agent is not stably associated with a delivery vehicle.
24. The composition of claim 22 wherein the therapeutic agent is stably associated with a delivery vehicle.
25. The composition of claim 21 wherein the delivery vehicles have a mean diameter in the range of 50-300 nm.
26. The composition of claim 22 wherein the delivery vehicles have a mean diameter in the range of 50-300 nm.
27. A method to impart drug sensitivity and/or administer treatment to a patient which method comprises administering to said patient an effective amount of the composition of claim 1.
28. A method to impart drug sensitivity to a subject which method comprises administering to a subject in need of such drug sensitivity a composition comprising a first drug resistance modulators stably associated with a first delivery vehicle and a composition comprising a second resistance modulator stably associated with a second delivery vehicle wherein said first and second drug resistance modulators are administered at a ratio that is non-antagonistic and wherein the pharmacokinetics of the drug delivery vehicles in the first and second compositions are coordinated.
29. A method to administer a treatment to a subject in need of such treatment which method comprises administering to said subject a composition comprising a therapeutic agent stably associated with a first delivery vehicle and a drug resistance modulator stably associated with a second delivery vehicle at a ratio wherein said therapeutic agent and drug resistance modulator are non-antagonistic and wherein the pharmacokinetics of the first and second delivery vehicles are coordinated.

30. The composition of claim 2 wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 1%-99% of the cells are affected ($f_a = 0.01-0.99$) in an *in vitro* assay for cytotoxicity or cytostasis.

31. The composition of claim 30 wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 10-90% of the cells are affected ($f_a = 0.1-0.9$) in an *in vitro* assay for cytotoxicity or cytostasis.

32. The composition of claim 31 wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 20-80% of the cells are affected ($f_a = 0.2-0.8$) in an *in vitro* assay for cytotoxicity or cytostasis.

33. The composition of claim 32 wherein said synergistic effect is exhibited over at least 20% of the concentration range such that 20-80% of the cells are affected in an *in vitro* assay for cytotoxicity or cytostasis.

34. The method of claim 28 wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 1%-99% of the cells are affected ($f_a = 0.01-0.99$) in an *in vitro* assay for cytotoxicity or cytostasis.

35. The method of claim 34 wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 10-90% of the cells are affected ($f_a = 0.1-0.9$) in an *in vitro* assay for cytotoxicity or cytostasis.

36. The method of claim 35 wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 20-80% of the cells are affected ($f_a = 0.2-0.8$) in an *in vitro* assay for cytotoxicity or cytostasis.

37. The method of claim 36 wherein said synergistic effect is exhibited over at least 20% of the concentration range such that 20-80% of the cells are affected in an *in vitro* assay for cytotoxicity or cytostasis.

38. The method of claim 29 wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 1%-99% of the cells are affected ($f_a = 0.01-0.99$) in an *in vitro* assay for cytotoxicity or cytostasis.

39. The method of claim 38 wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 10-90% of the cells are affected ($f_a = 0.1-0.9$) in an *in vitro* assay for cytotoxicity or cytostasis.

40. The method of claim 39 wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 20-80% of the cells are affected ($f_a = 0.2-0.8$) in an *in vitro* assay for cytotoxicity or cytostasis.

41. The method of claim 40 wherein said synergistic effect is exhibited over at least 20% of the concentration range such that 20-80% of the cells are affected in an *in vitro* assay for cytotoxicity or cytostasis.